REMARKS

Entry of the foregoing, and further and favorable consideration of the subject application on the merits is respectfully requested.

By the present Amendment, claims 34 and 45 have been canceled without prejudice to or disclaimer of any of the subject matter claimed therein. Applicants reserve their right to file a continuation application directed towards the canceled subject matter. Claims 32, 38, 42, 43 and 49 have been amended. Support for the amendments to claims 32 and 43 and for new claims 53 to 60 can be found in the specification at least on page 15, lines 23 to 31; on page 16, lines 5 to 11; in Example 1 (page 29, lines 5 to 12) and in Example 4 (page 33 lines 14-19 and page 35 lines 1-6) and in Figure 1.3. The amendment to claim 42 merely changed the dependency of the claim. New claims 53-60 have been added. No new matter has been added.

Turning now to the Official Action, Applicants gratefully acknowledge the indication, at page 4 of the Official Action, that claims 39 to 41 and 50 to 52 are free of the prior art, and at page 1 of the Official Action, that they are allowable.

Claim Rejections - 35 USC §103

Claims 32, 34, 38, 42, 43, 45 and 49 remain rejected under 35 USC 103(a) as purportedly unpatentable over Fitzmaurice *et al.* and Masuta *et al.* in view of Grierson *et al.* for the reasons of record set forth in the Official Action mailed 12-14-01 and further in view of Kumagai *et al.* and Routh *et al.* for the reasons set forth in the Official action mailed 06-27-03. This rejection is respectfully traversed.

The Examiner maintains, at page 2 of the Official Action, that the prior art provides both motivation and an expectation of success for using satellite viruses as vectors for silencing of endogenous genes. Applicants respectfully submit that the presently claimed invention is not obvious over either Fitzmaurice *et al.* and Masuta et al. alone, or in combination with Grierson *et al.*, Kumagai *et al.* and Routh *et al.*

In the previous Official Action, at page 3, the Examiner addressed Applicants' arguments regarding the lack of expectation of success.

> Moreover, Applicants argue that prior to the filing of the present invention the use of satellite vectors as silencing vectors was generally doubted by person skilled in the art, as such vectors were believed to be unstable and as satellite viruses were known to have a high mutation rate. In regards to Applicants' allegation regarding unpredictability associated with the use of satellite vectors as silencing vectors, Applicants have not provided any credible evidence to substantiate their allegation of non-enablement with regards to the expectation of success for modifying Fitzmaurice et al. and Masuta et al. with the teachings of Grierson into the vectors of the present invention.

In response, Applicants provided evidence, in the form of publications by Simon, and by Qiu et al., a Declaration of Dr. Frank Meulewaeter, supporting their argument that Masuta et al. does not pertain to satellite viruses, as recited in the present claims, but to satellite RNA. At page 2 of the outstanding Official Action, the Examiner notes Applicants' arguments, and the substance of the declaration of Dr. Meulewaeter. However, the Examiner has provided no rebuttal to Applicants' arguments with regard to the Masuta et al. publication. Accordingly, Applicants respectfully submit that the present rejection is unsustainable to the extent that it continues to rely on the Masuta et al. publication.

In their previous response Applicants also provided evidence, in support of their arguments regarding the Fitzmaurice publication cited by the Examiner. This evidence took the form of publications by Mirkov et al., and Routh et al., both of which highlight potential problems associated with STMV-based vectors, such as accumulation of mutations and recombination between the vector and the helper virus genome. At page 3 of the Official Action, the Examiner notes that "none of the cited references were used to support the present rejection." This is hardly surprising, as the cited references in question do not support, but rather undermine, the present rejection.

The Examiner further notes, at pp 3-4 of the Official Action, that "although several of the cited references teach that there is a high level of heterogeneity in the STMV genome, there is no direct evidence that high heterogeneity is common among all satellite RNA viruses, and there is no comparison set forth between non-satellite RNA viruses and other satellite viruses." However, the Examiner is required

to evaluate Applicants' objective evidence (in this case, evidence of heterogeneity) against the evidence supporting the rejection, *i.e.*, evidence of homogeneity among satellite RNA viruses. *See,* MPEP 716.01(d). The Examiner has pointed to no such evidence. Applicants respectfully submit that their unrebutted evidence of nonobviousness is entitled to considerably more weight that that apparently accorded by the Examiner.

At page 3 of the Official Action, the Examiner argues that "none of the cited references generically suggest that satellite RNA viruses should not be used as vectors for silencing of endogenous plant genes." However, Applicants did not argue that the cited publications made such a generic suggestion. Instead, Applicants cited the publications to provide objective evidence that one of ordinary skill would not have a reasonable expectation of success in modifying the teachings of the publications cited by the Examiner in order to arrive at the presently claimed invention.

In view of the foregoing, Applicants respectfully submit that the arguments and evidence submitted with their prior response have successfully rebutted the Examiner's contention that the present claims are *prima facie* obvious over the publications cited by the Examiner. Nevertheless, Applicants offer the following comments to the Examiner's most recent arguments.

The Examiner asserts, at pp. 2-3 of the Official Action, that Fitzmaurice *et al.* "provides a recombinant expression system for modifying the genome of a satellite RNA virus, satellite tobacco mosaic virus, for the introducing heterologous RNA into plant cells, wherein the exogenous RNA segment may also be sense or antisense." However, neither Fitzmaurice *et al.* nor Grierson *et al.*, Kumagai *et al.* or Routh *et al.* disclose or suggest that vectors derived from STMV that encode an origin of assembly of TMV and wherein part or all of the coat protein encoding gene of STMV is deleted can be used for the introduction of inhibitory RNA in the cytoplasm of plant cells, as required by the present claims.

Masuta *et al.* suggests the use of satellite RNAs of plant viruses as vectors for expressing proteins or expressing antisense sequences of viruses. In contrast, the present claims are drawn to vectors derived from satellite RNA viruses STMV and

STNV, and not to vectors derived from satellite RNAs of plant viruses. There is thus no motivation provided by the cited publications to modify the disclosure of the Masuta *et al.* publication or to combine it with the disclosures of Grierson *et al.*, Kumagai *et al.* and Routh *et al.* to arrive at the presently claimed invention. Nor does Masuta *et al.* provide one of ordinary skill in the art with the requisite reasonable expectation of success for one of ordinary skill in the art to make such modifications and/or combinations in order to arrive at the presently claimed methods and kits.

Grierson *et al.* discloses constructs that comprise both an antisense and a sense portion, wherein upon transcription said constructs yield inhibitory RNA, which comprises both a sense and an antisense region. However, Grierson *et al.* neither discloses nor suggests that vectors derived from STMV that encode an origin of assembly of TMV and wherein part or all of the coat protein encoding gene of STMV is deleted can be used for the introduction of inhibitory RNA in the cytoplasm of plant cells. The Grierson *et al.* publication likewise fails to provide either motivation or a reasonable expectation of success for one of ordinary skill in the art that said vectors can be used for the introduction of inhibitory RNA in the cytoplasm of plant cells.

The Examiner asserts, at p. 3 of the Official Action, that "Routh *et al.* provides functional studies where several distinct regions of the STMV genome are deleted and the mutant remain biologically active with the aid of its helper virus." From this, the Examiner argues, "Routh et al. concludes that the STMV a satellite virus 'may be a good candidate for the use as a broad host range expression vector.' (see page 126, last paragraph)."

However, Routh *et al.* also states that "deletions and frameshift mutations in the coat protein open reading frame resulted in decreased accumulation of STMV RNA" and that "the mild symptoms induced in tobacco by co-inoculations of wild-type STMV/TMGMV or infection with TMGMV alone were altered to severe systemic necrosis when plants were co-inoculated with these STMV coat protein mutants and TMGMV" (at least in the abstract). Applicants submit that one of ordinary skill in the art would therefore not have had a reasonable expectation of success and would not have been motivated to delete part or all of the coat protein encoding gene of STMV considering that such modifications may lead to much less vector RNA and necrosis

phenotypes, which would make it very unlikely that a gene silencing phenotype would be induced or, if induced, would not be masked by a necrosis phenotype.

The Examiner further argues, at page 3 of the Official Action, that "Kumagai *et al.* provides a method for conferring disease resistance in plant host comprising the use of viral expression vectors (col. 2, lines 30-39)" wherein said viral expression vectors "are preferably derived from RNA plant viruses, and furthermore wherein said RNA plant virus is an RNA satellite virus such as tobacco necrosis satellite virus, see col. 3, lines 60-61." The Examiner argues that it would have been obvious to one of ordinary skill in the art at the time of filing to modify the teachings of Fitzmaurice *et al.* and Masuta *et al.* with the teachings of Grierson *et al.*, Kumagai *et al.* and Routh *et al.* and that the one of ordinary skill in the art would have been motivated to use satellite RNA viruses to design gene silencing vectors since the disclosure of Kumagai *et al.* expressly states that the disclosed viral expression vectors, which include satellite RNA viruses, can be used specifically to design gene silencing/knock out systems in order to confer herbicide or pathogen resistance to plants (col.16-17).

However, Kumagai *et al.*(col. 16-17) describes the construction of a genomic DNA library in a recombinant viral nucleic acid vector, Kumagai *et al.* does not teach the use of satellite tobacco mosaic virus comprising an origin of assembly of tobacco mosaic virus wherein part or all of the coat protein encoding gene is deleted for the introduction of inhibitory RNA in the cytoplasm of plant cells.

Therefore, Applicants submit that the combined teachings of Fitzmaurice *et al.*, Masuta *et al.*, Grierson *et al.*, Kumagai *et al.* and Routh *et al.* do not provide motivation nor a reasonable expectation of success that satellite RNA viruses, such as STMV, modified to comprise an origin of assembly of TMV and wherein part or all of the coat protein encoding gene is deleted, could be successfully used for introduction of inhibitory RNA into the cytoplasm of plant cells.

In view of the lack of a reasonable expectation of success, and of a motivation to combine the teachings of the cited publications, Applicants respectfully submit that the presently claimed invention is not *prima facie* obvious over the cited publications. Withdrawal of this rejection is thus respectfully requested.

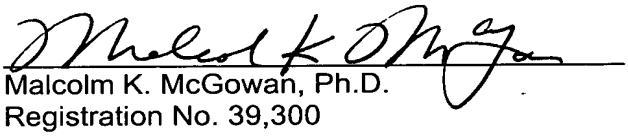
From the foregoing, favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is respectfully requested.

In the event that there are any questions concerning this Amendment, or the Application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: October 24, 2003

By: 
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